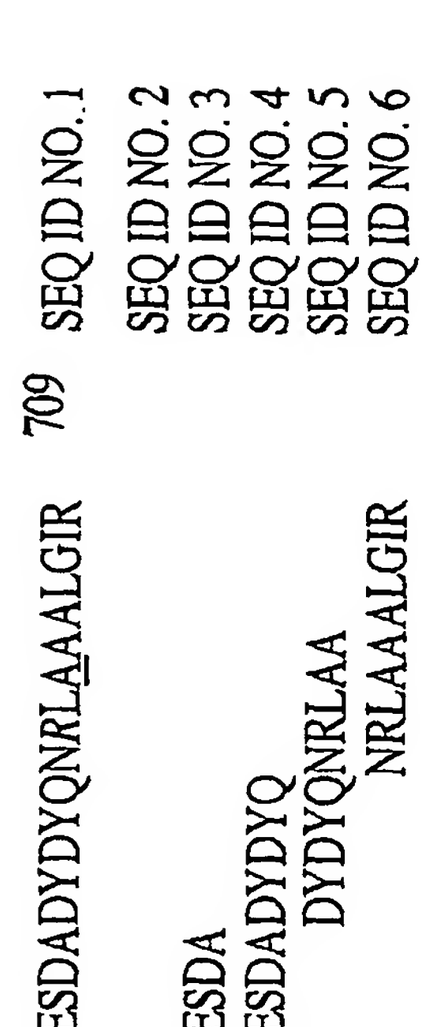


FIG. 1

BEST AVAILABLE COPY

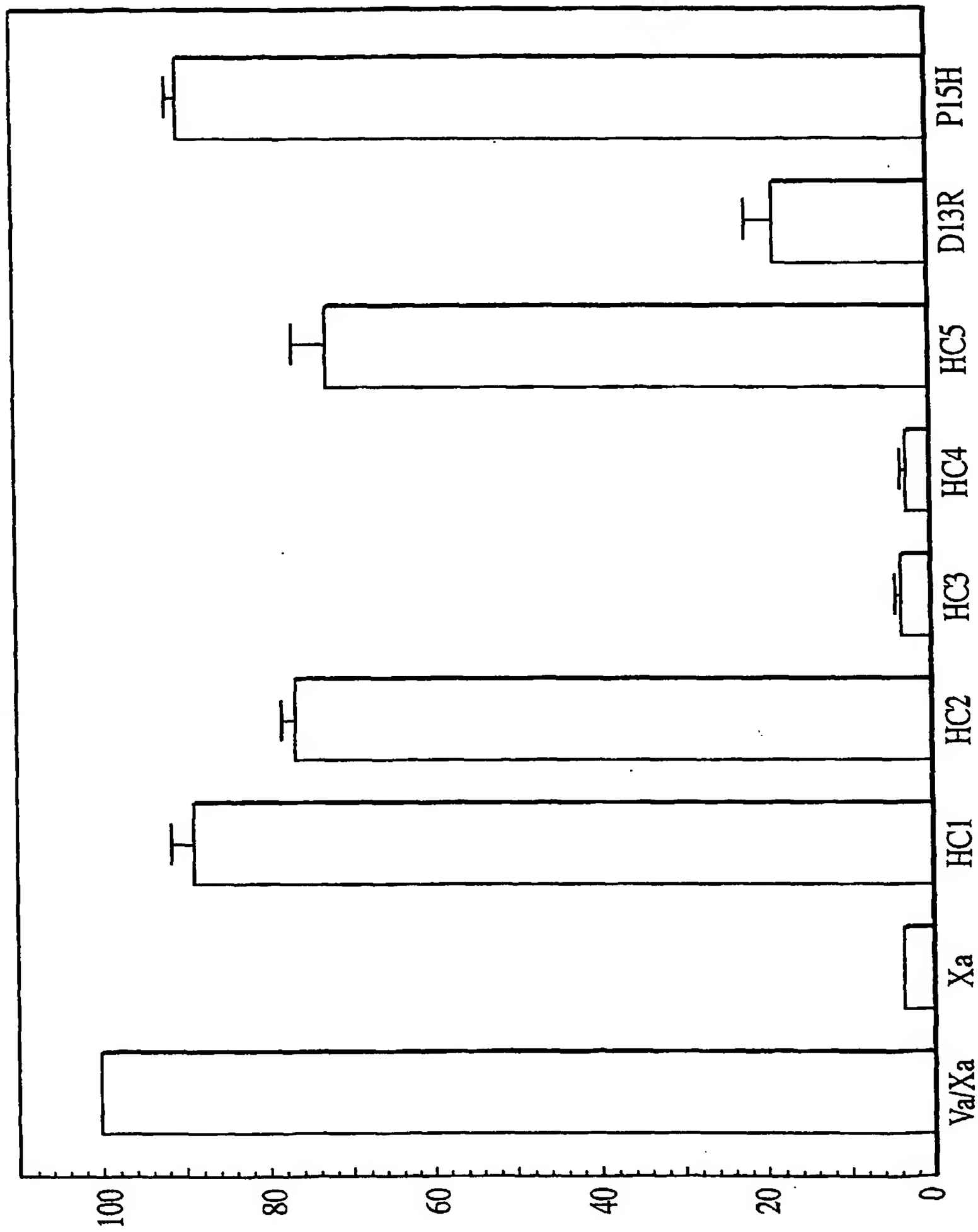

P15H
D13R
HC5
HC4
HC3
HC2
HC1
Xa
Va/Xa
100
80
60
40
20
0
% COFACTOR ACTIVITY

FIG. 2A

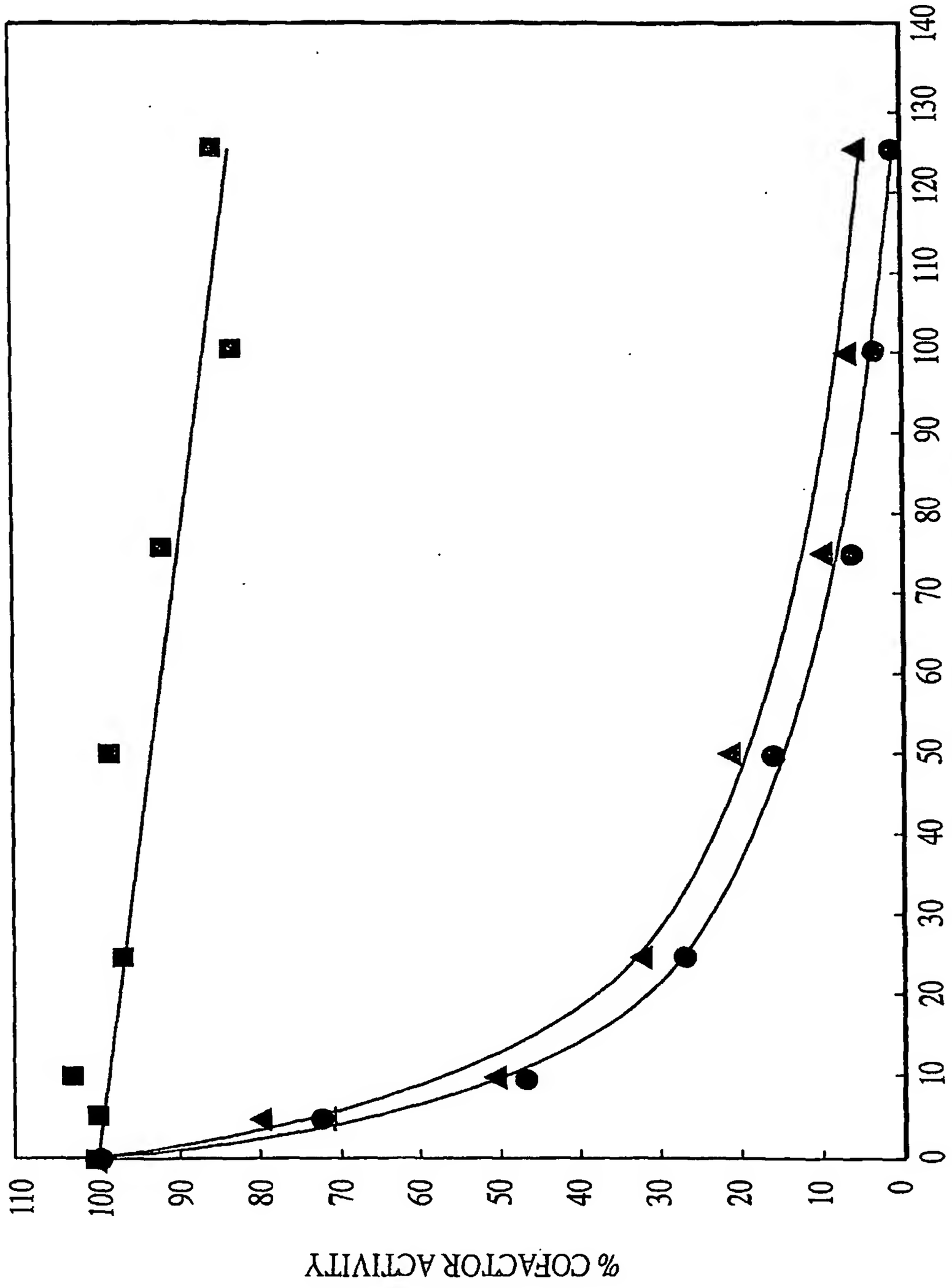

% COFACTOR ACTIVITY
110
100
90
80
70
60
50
40
30
20
10
0
0
10
20
30
40
50
60
70
80
90
100
110
120
130
140
PEPTIDE CONCENTRATION (μM)

FIG. 2B

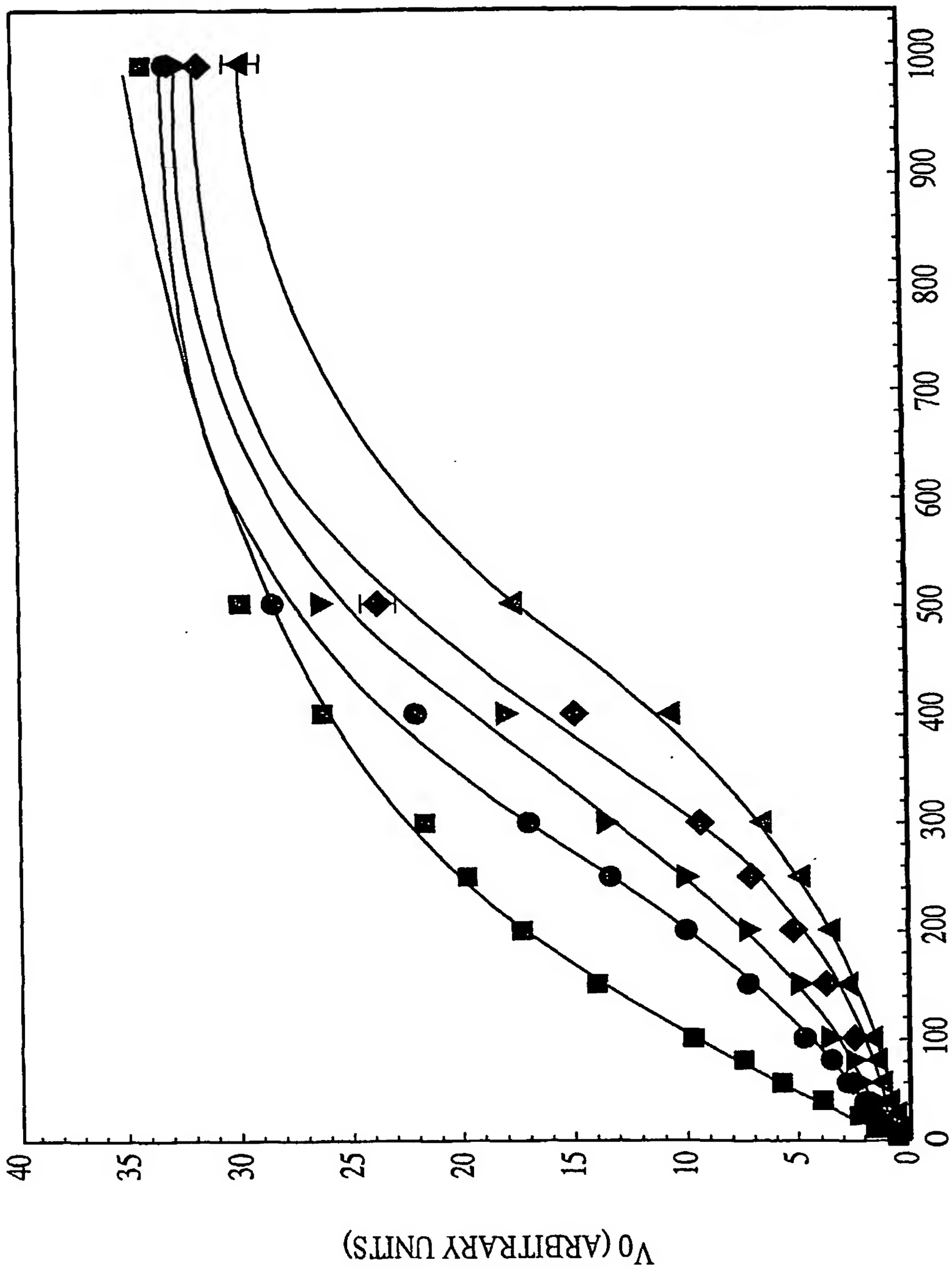

V_0 (ARBITRARY UNITS)
0
5
10
15
20
25
30
35
40
PROTHROMBIN (nM)
0
100
200
300
400
500
600
700
800
900
1000

FIG. 2C

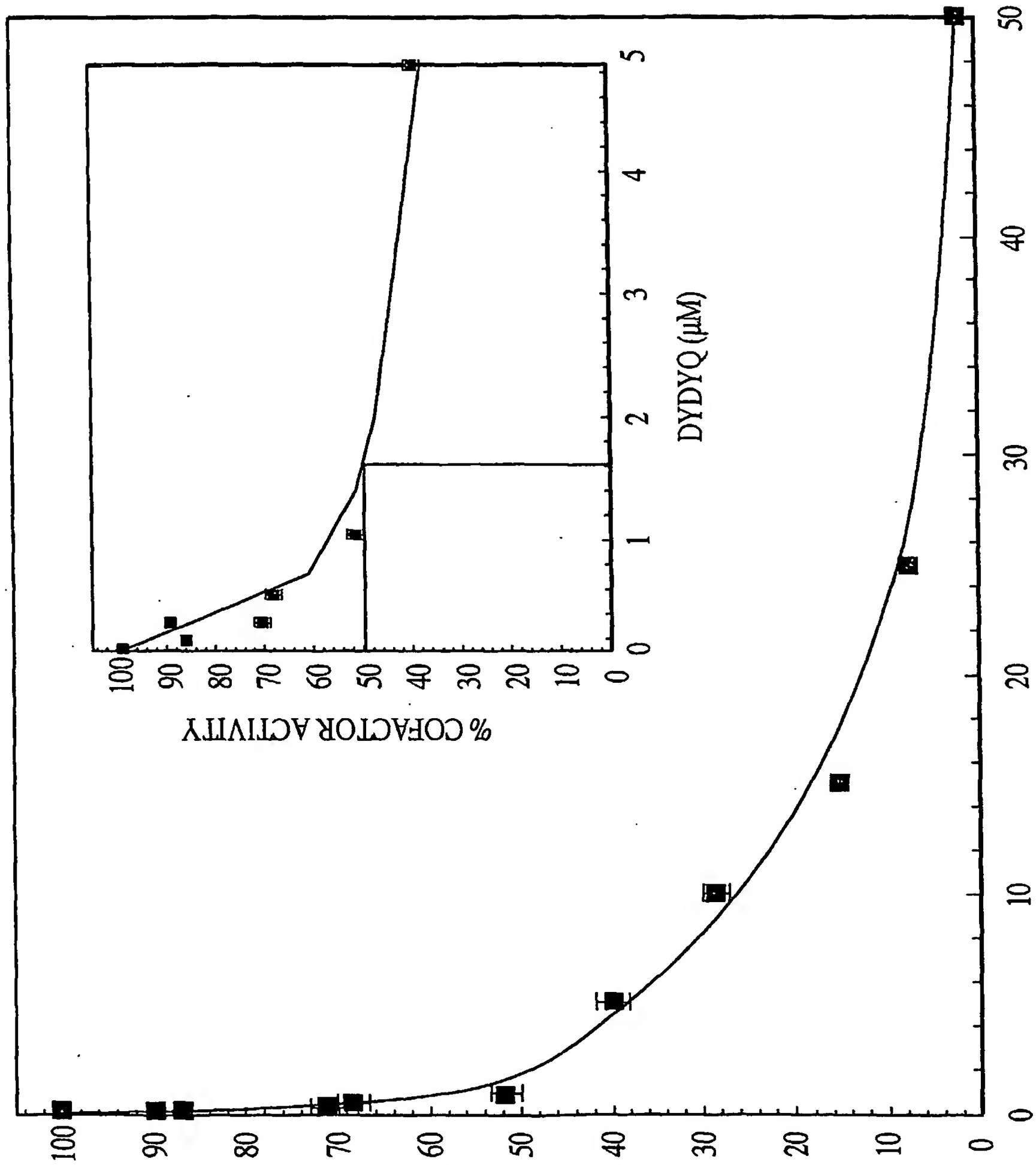

% COFACTOR ACTIVITY
100
90
80
70
60
50
40
30
20
10
0
DYDYQ (μM)
0
1
2
3
4
5
% COFACTOR ACTIVITY
100
90
80
70
60
50
40
30
20
10
0
PEPTIDE CONCENTRATION (μM)
0
10
20
30
40
50

FIG. 3A

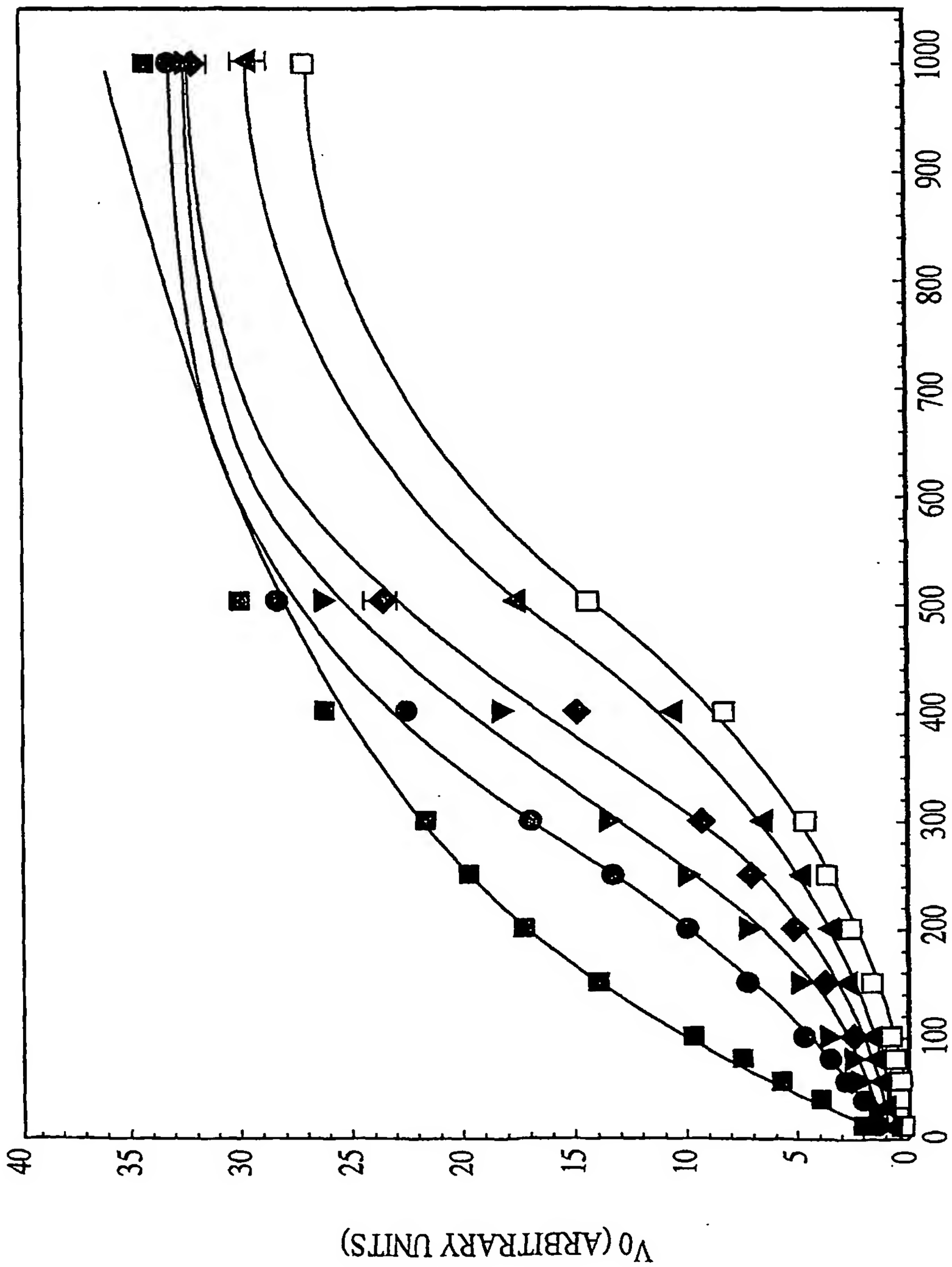

V_0 (ARBITRARY UNITS)
40
35
30
25
20
15
10
5
0
0
100
200
300
400
500
600
700
800
900
1000
PROTHROMBIN (nM)

FIG. 3B

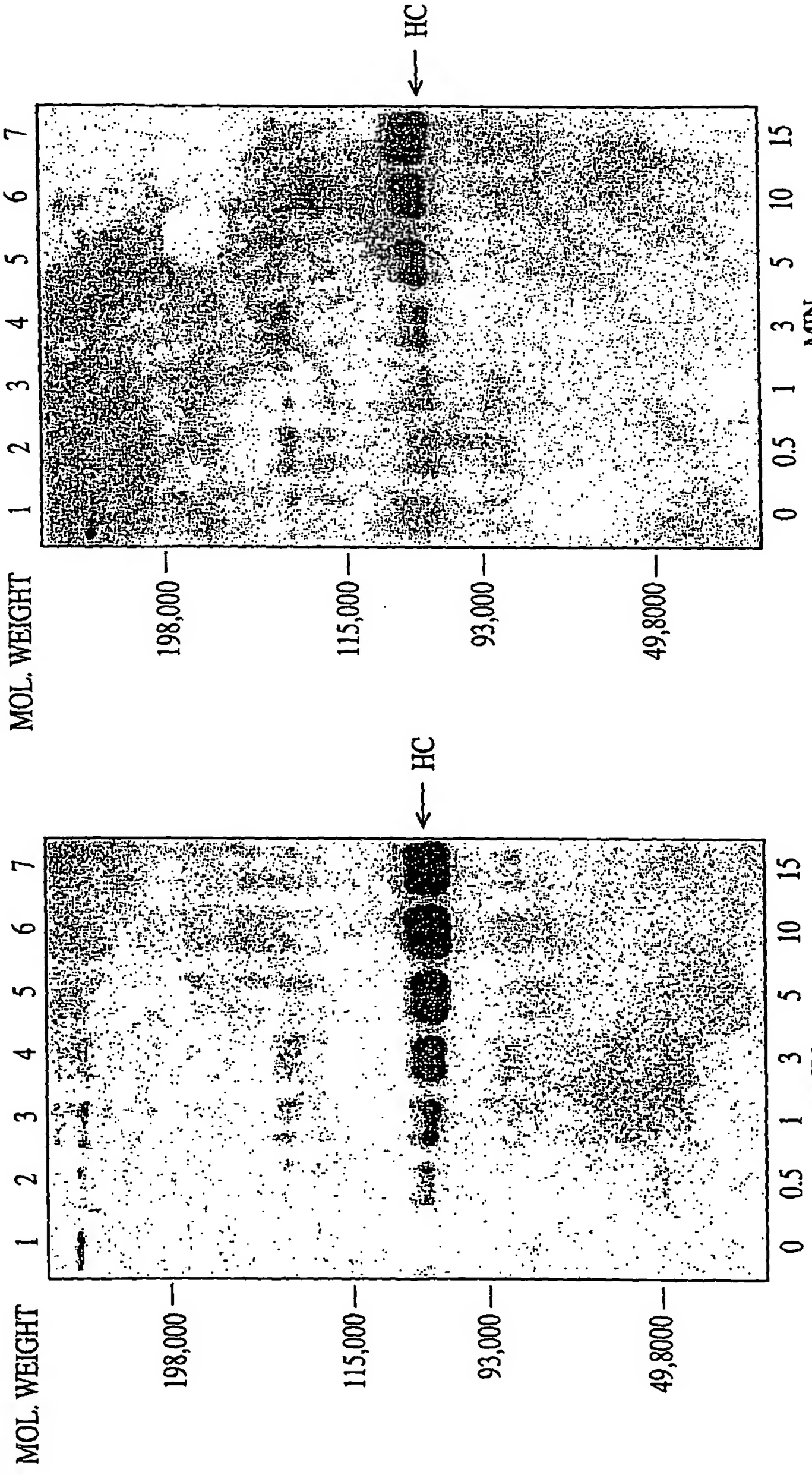

HC
MOL. WEIGHT
198,000
115,000
93,000
49,8000
1 2 3 4 5 6 7
0 0.5 1 3 5 10 15
MIN

FIG. 4B

HC
MOL. WEIGHT
198,000
115,000
93,000
49,8000
1 2 3 4 5 6 7
0 0.5 1 3 5 10 15
MIN

FIG. 4A

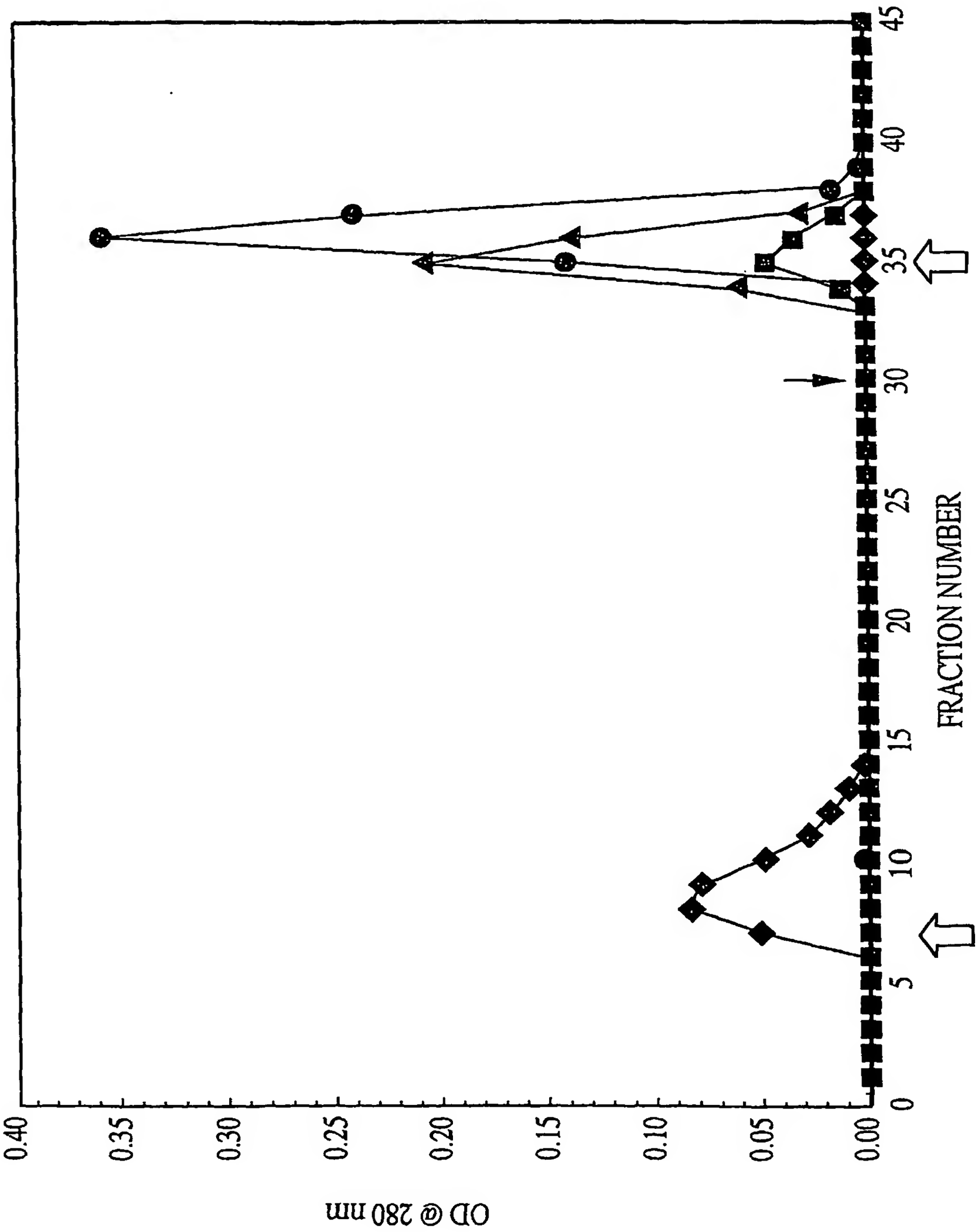

OD @ 280 nm
0.40
0.35
0.30
0.25
0.20
0.15
0.10
0.05
0.00
0
5
10
15
20
25
30
35
40
45
FRACTION NUMBER

FIG. 5

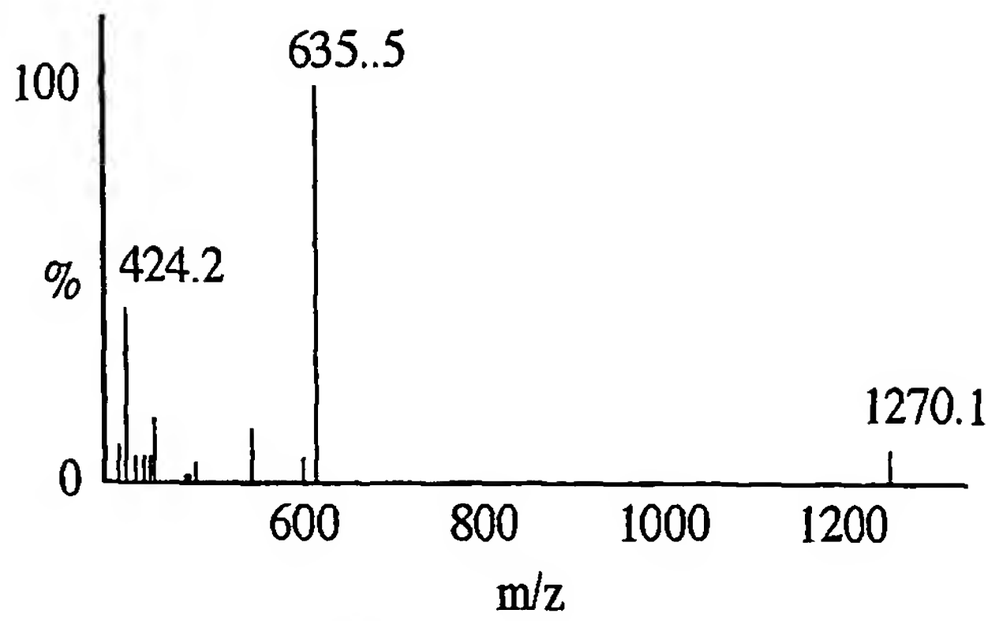


FIG. 5A

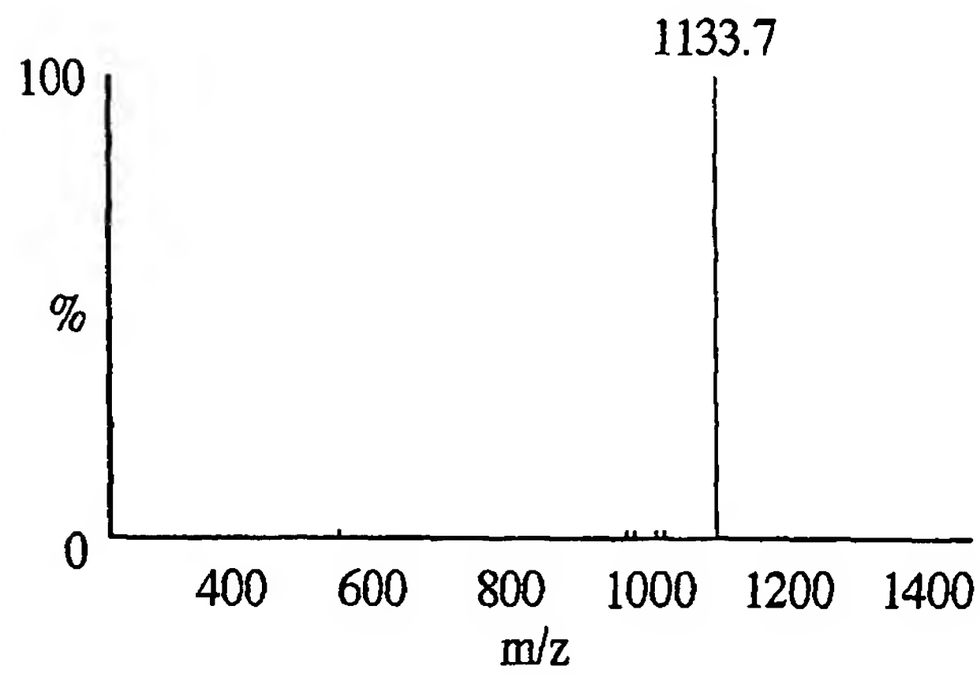


FIG. 5B

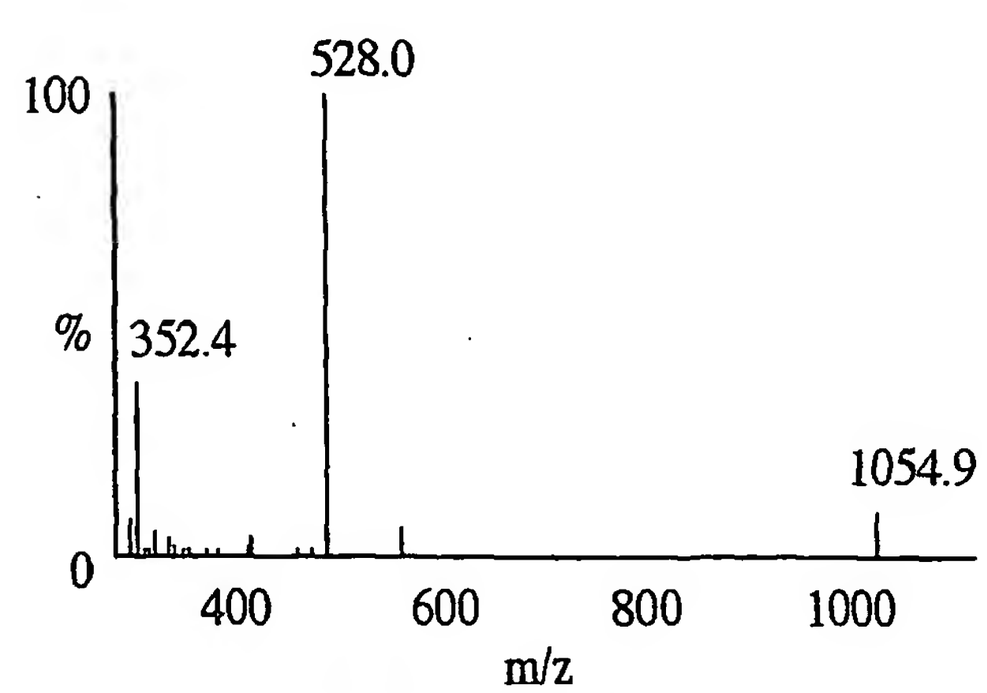


FIG. 5C

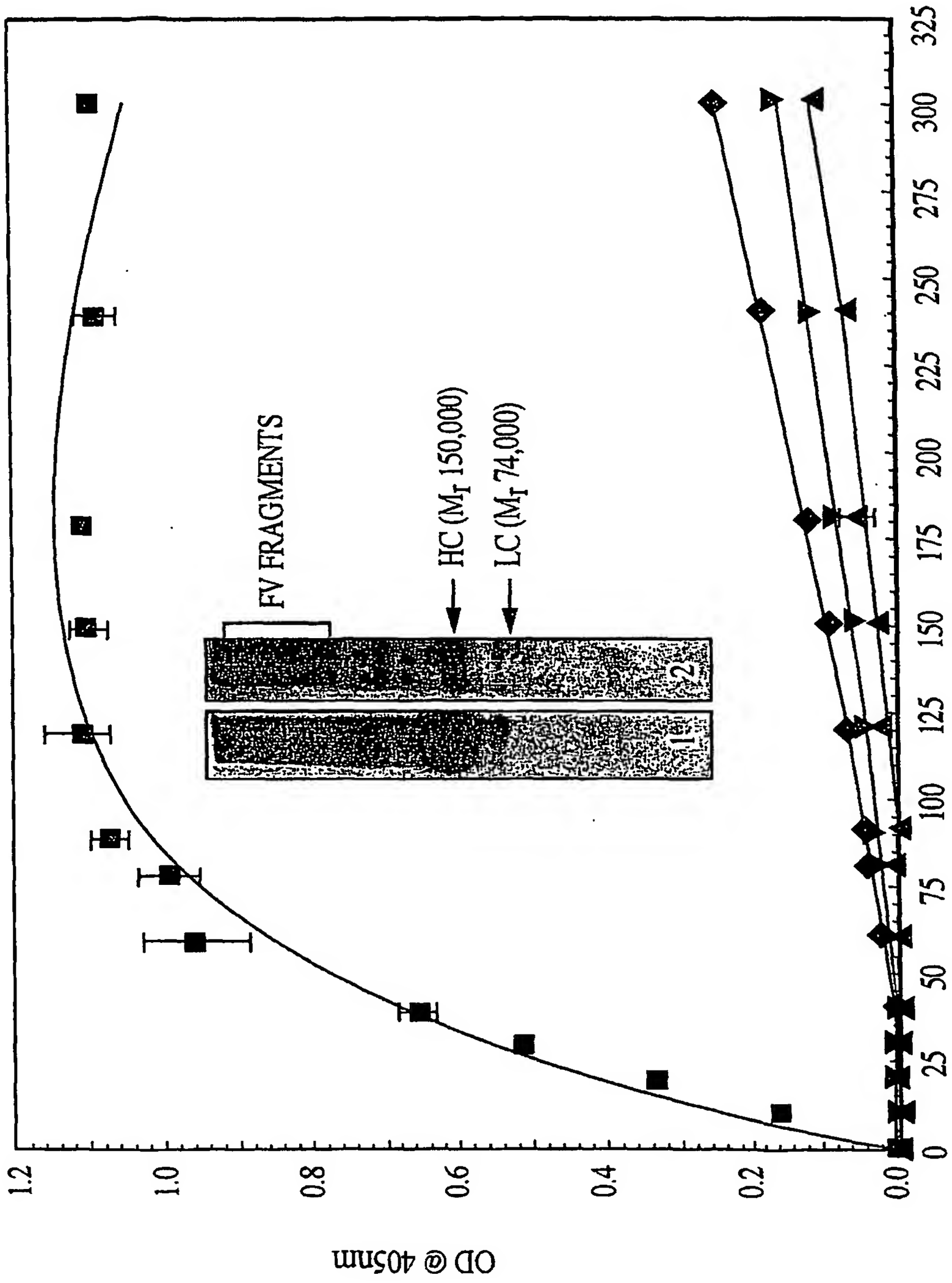

OD @ 405nm
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
25
50
75
100
125
150
175
200
225
250
275
300
325
SECONDS
FV FRAGMENTS
HC (M_r 150,000)
LC (M_r 74,000)
12
11

FIG. 6A

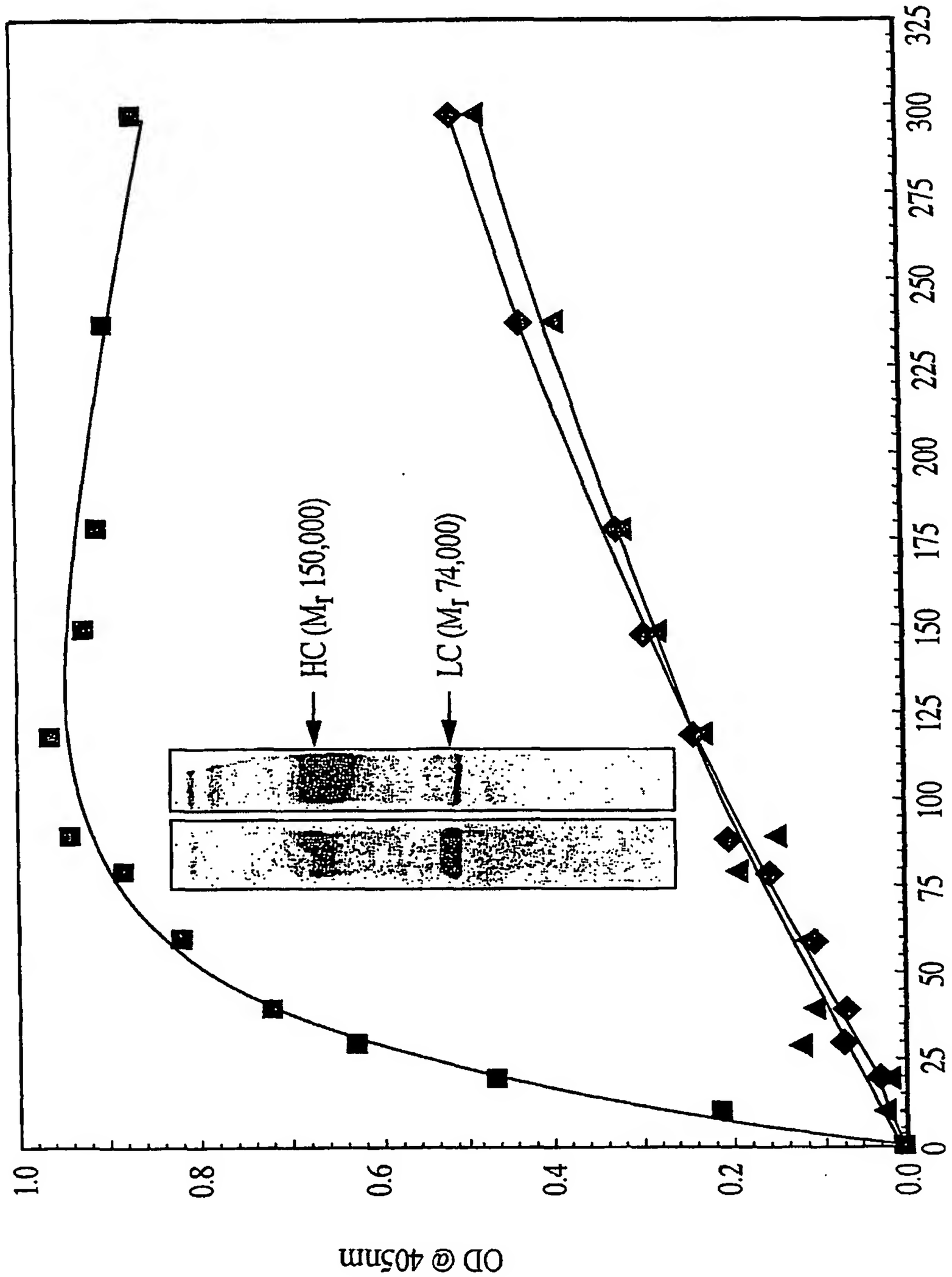

OD @ 405nm
1.0
0.8
0.6
0.4
0.2
0.0
0
25
50
75
100
125
150
175
200
225
250
275
325
300
SECONDS
HC (M_r 150,000)
LC (M_r 74,000)

FIG. 6B

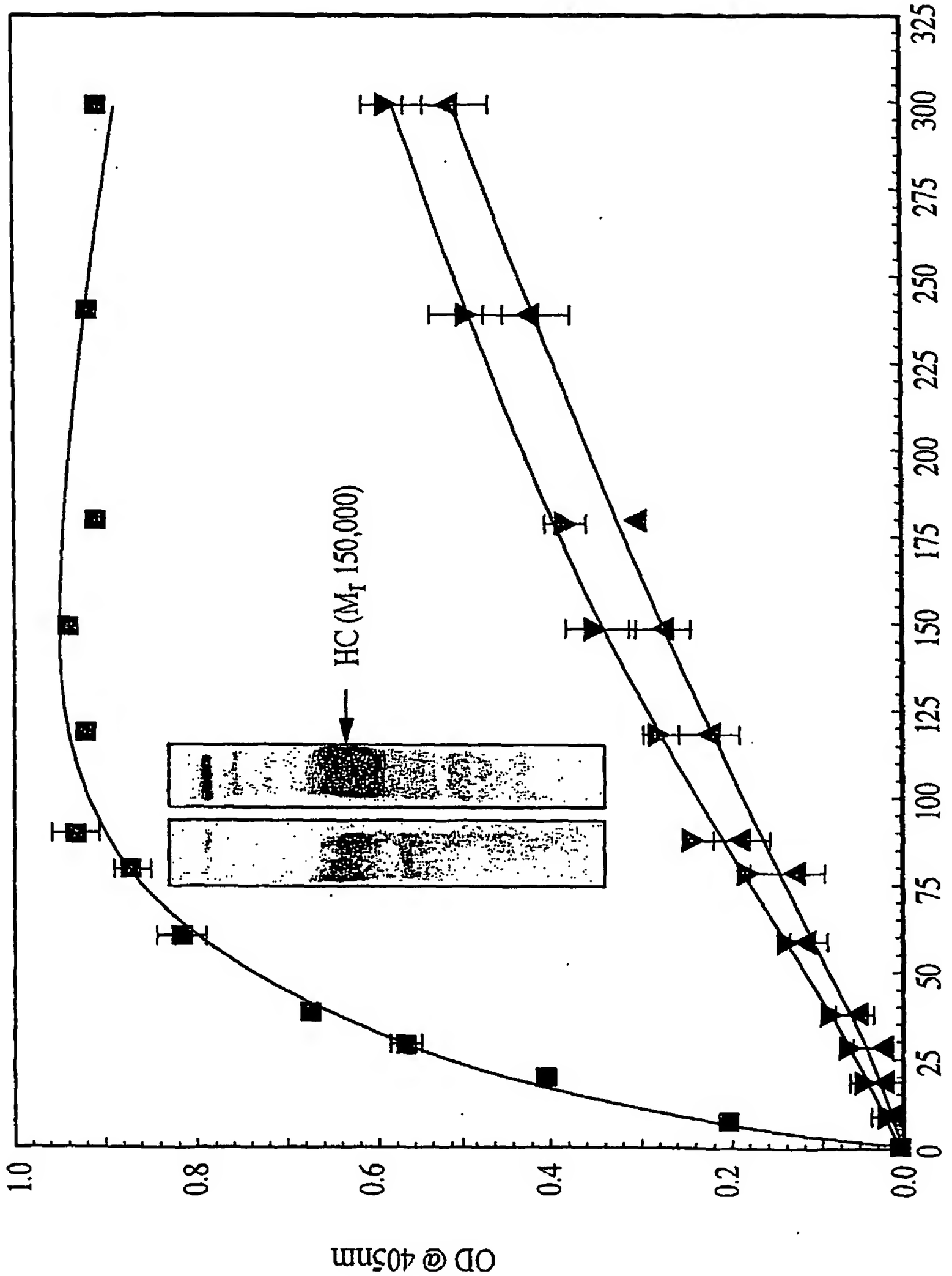

OD @ 405nm
1.0
0.8
0.6
0.4
0.2
0.0
0
25
50
75
100
125
150
175
200
225
250
275
300
325
SECONDS
HC (M_r 150,000)

FIG. 6C

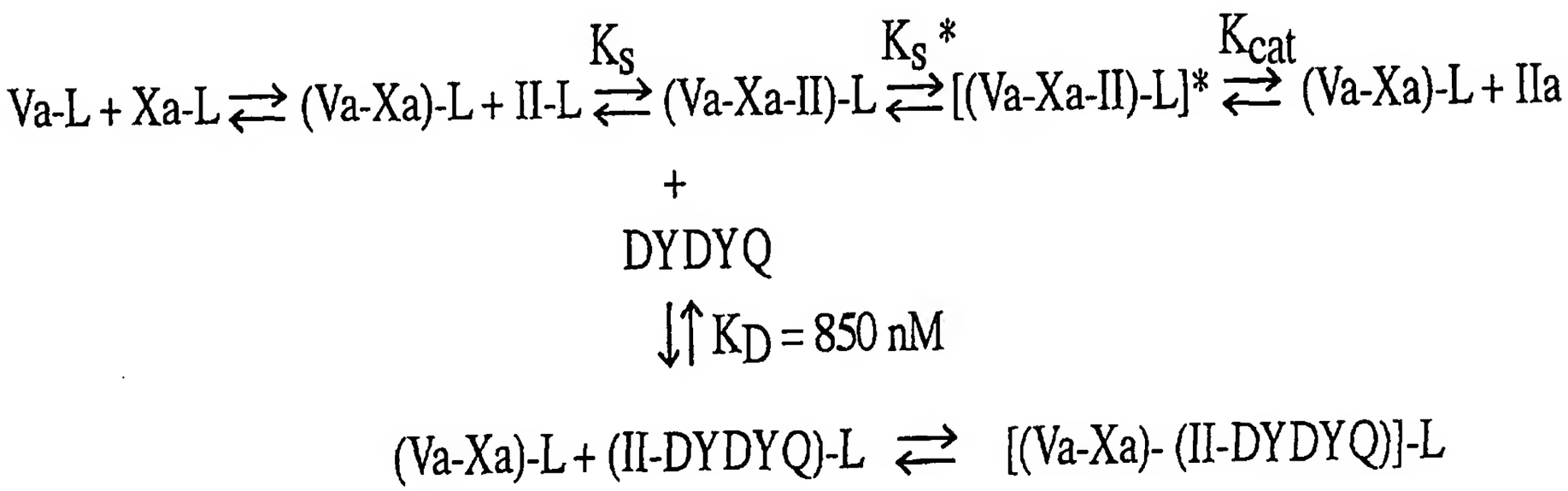
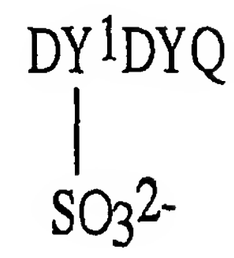
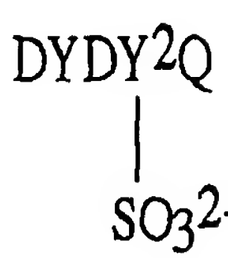

Va-L + Xa-L ⇄ (Va-Xa)-L + II-L ⇄ (Va-Xa-II)-L ⇄ [(Va-Xa-II)-L]* ⇄ (Va-Xa)-L + IIa
Ks
Ks *
Kcat
+
DYDYQ
↓↑ KD = 850 nM
(Va-Xa)-L + (II-DYDYQ)-L ⇄ [(Va-Xa)- (II-DYDYQ)]-L
Km = 0.39 ± 0.02 μM ≅ Ks
Kcat = Vmax(obs) / ET = 2.2 ± 0.12 s-1
Kcat / Km = 0.6 x 10^7 M-1s-1

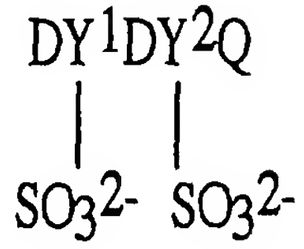
FIG. 7



(D5Q1) SEQ ID NO. 7



(D5Q2) SEQ ID NO. 8



(D5Q1,2) SEQ ID NO. 9

FIG. 8

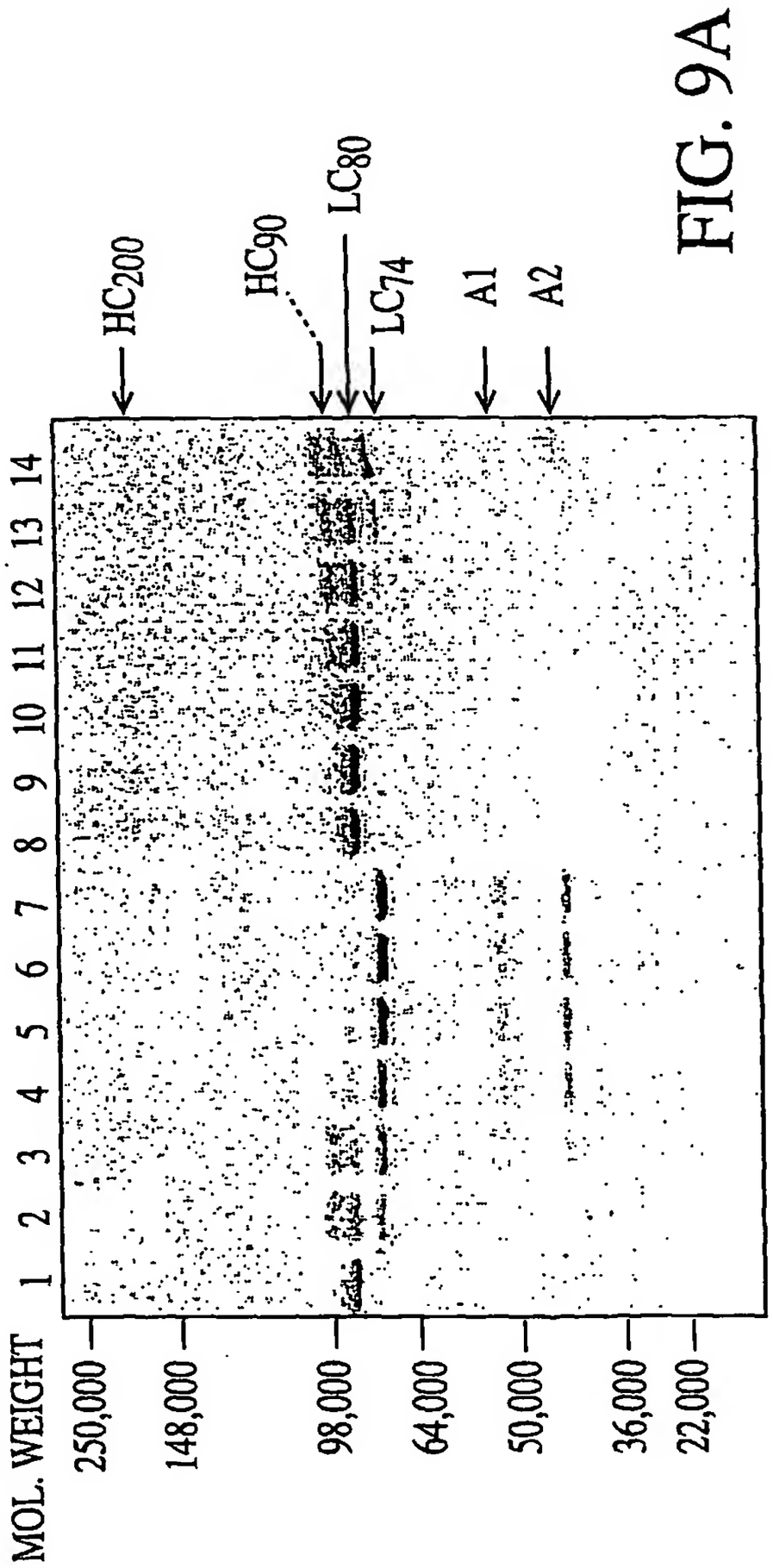

HC200
HC90
LC80
LC74
A1
A2
1 2 3 4 5 6 7 8 9 10 11 12 13 14
MOL. WEIGHT
250,000
148,000
98,000
64,000
50,000
36,000
22,000

FIG. 9A

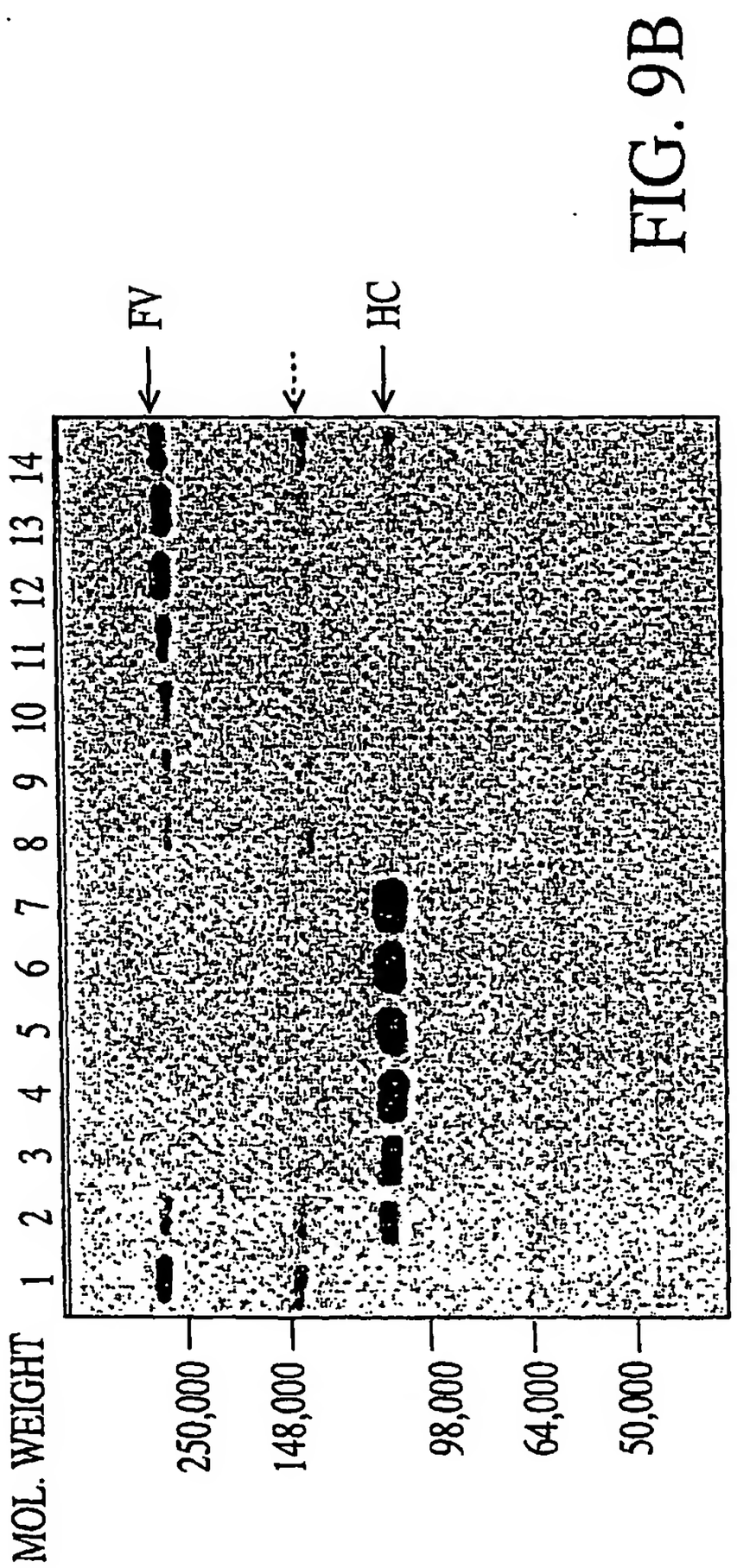

FV
HC
1 2 3 4 5 6 7 8 9 10 11 12 13 14
MOL. WEIGHT
250,000
148,000
98,000
64,000
50,000

FIG. 9B

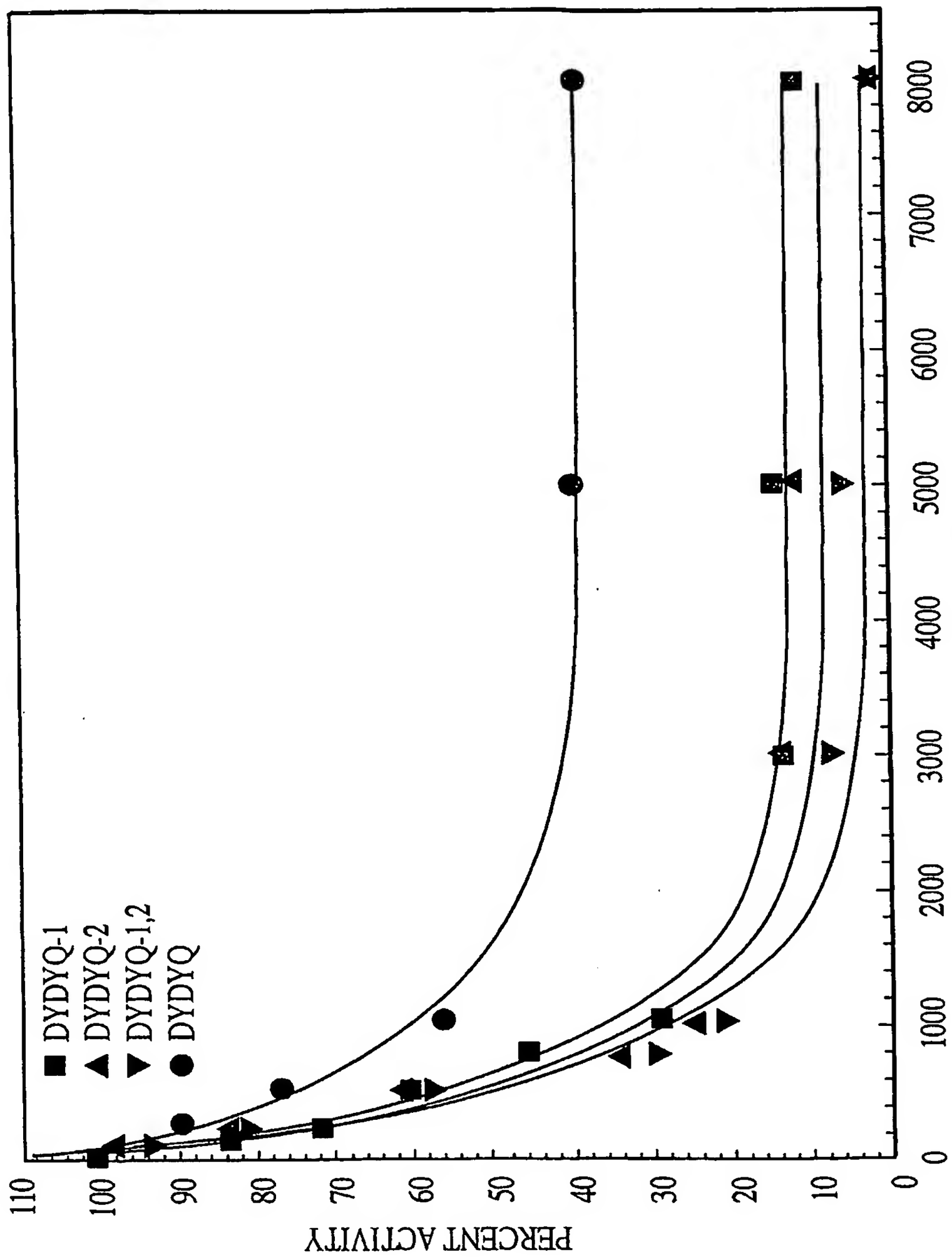

PERCENT ACTIVITY
110
100
90
80
70
60
50
40
30
20
10
0
0
1000
2000
3000
4000
5000
6000
7000
8000
(DYDYQ1,2 nM)
DYDYQ-1
DYDYQ-2
DYDYQ-1,2
DYDYQ

FIG. 10A

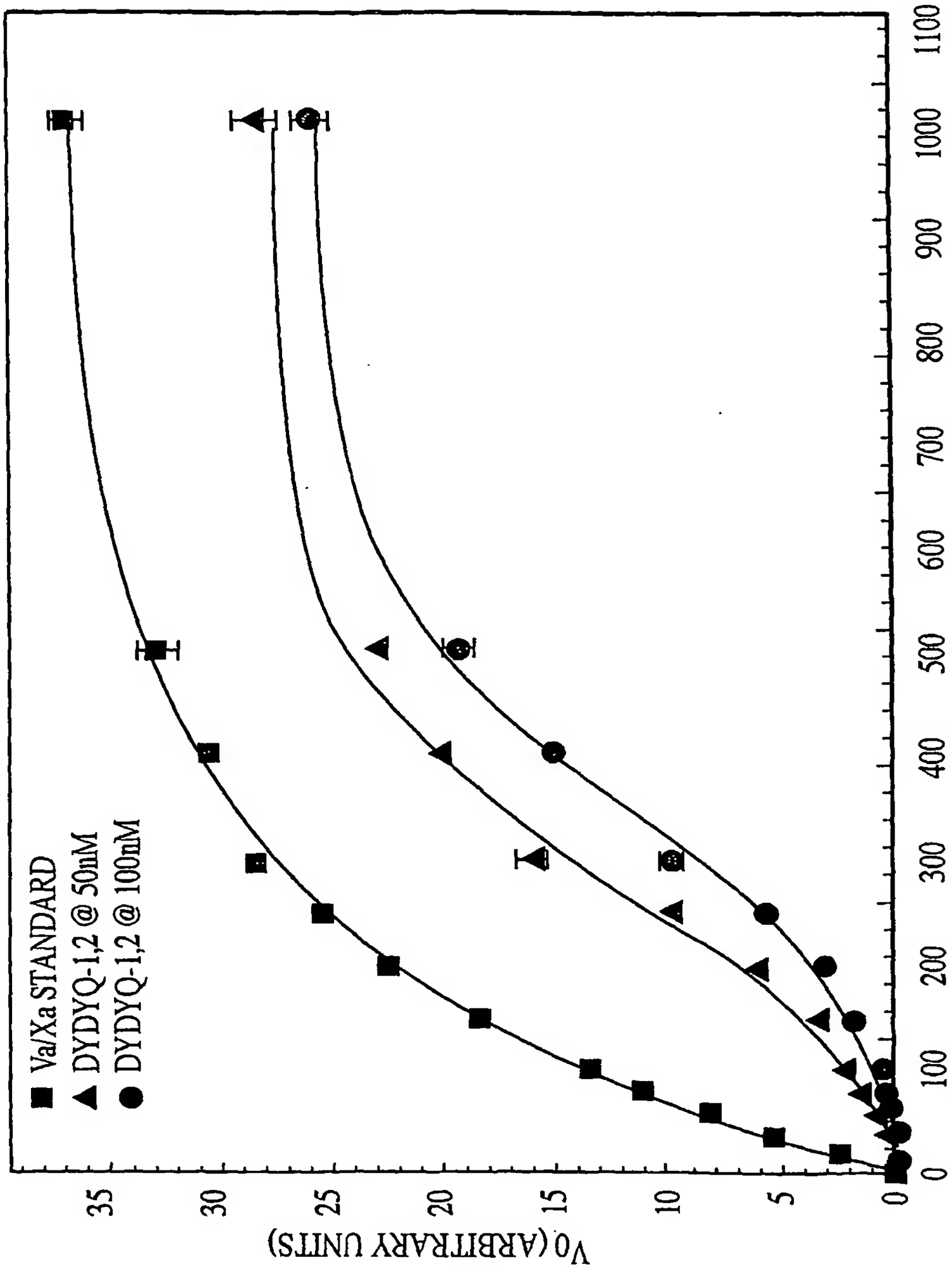

■ Va/Xa STANDARD
▲ DYDYQ-1,2 @ 50nM
● DYDYQ-1,2 @ 100nM
V_0 (ARBITRARY UNITS)
0
5
10
15
20
25
30
35
0
100
200
300
400
500
600
700
800
900
1000
1100
PROTHROMBIN (nM)

FIG. 10B

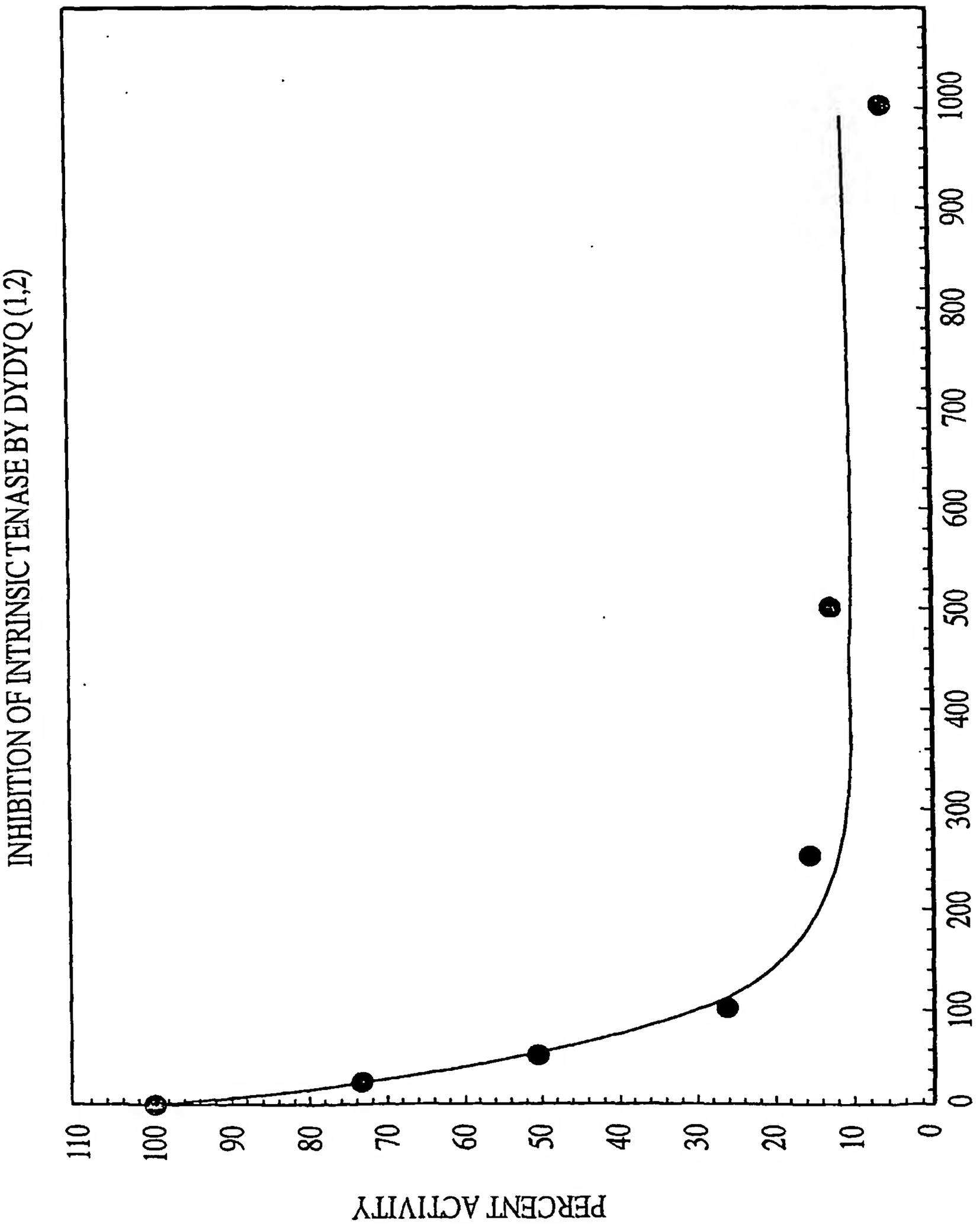

INHIBITION OF INTRINSIC TENASE BY DYDYQ (1,2)
PERCENT ACTIVITY
110
100
90
80
70
60
50
40
30
20
10
0
0
100
200
300
400
500
600
700
800
900
1000
(DYDYQ1,2 nM)

FIG. 11A

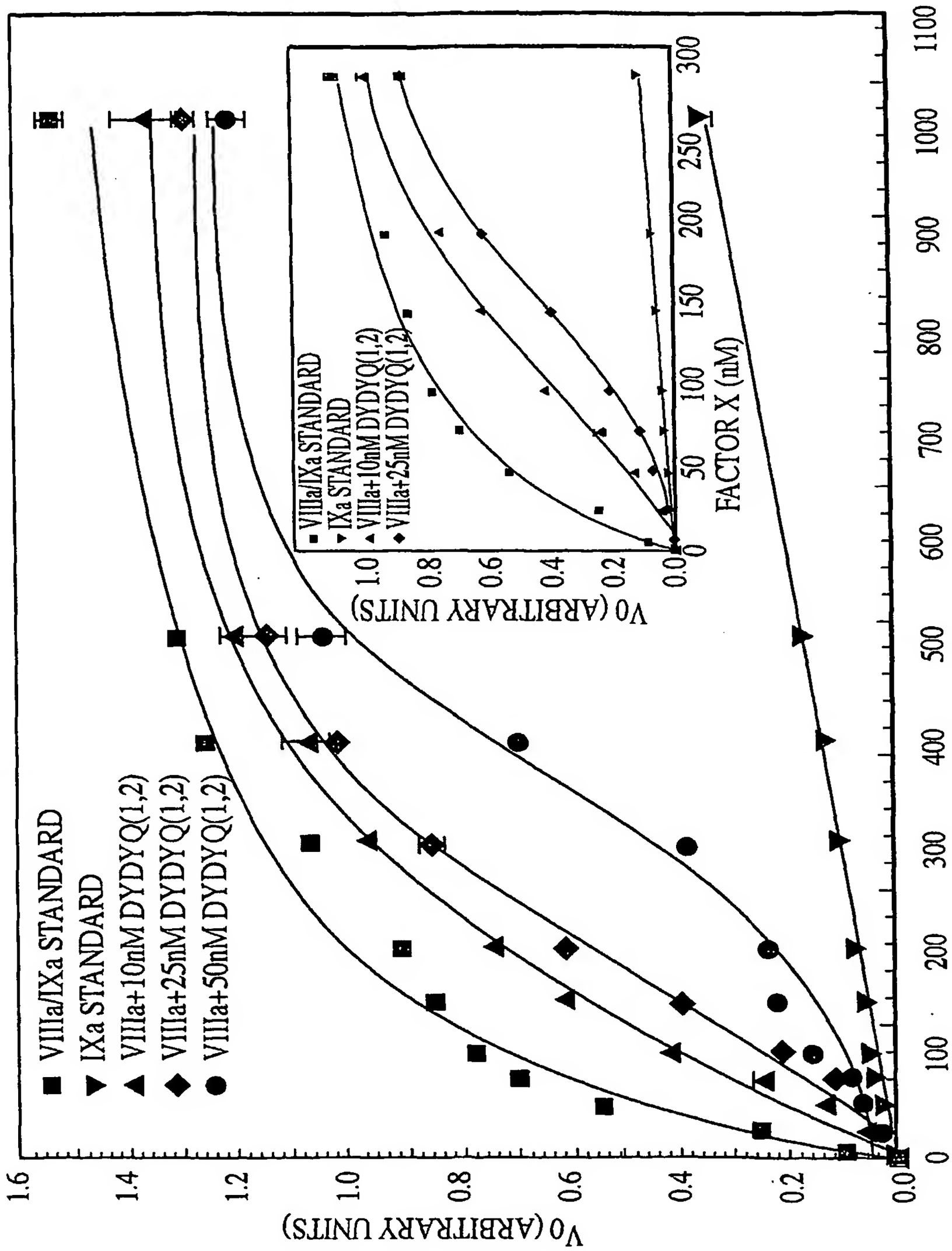

VIIIa/IXa STANDARD
IXa STANDARD
VIIIa+10nM DYDYQ(1,2)
VIIIa+25nM DYDYQ(1,2)
VIIIa+50nM DYDYQ(1,2)
V0 (ARBITRARY UNITS)
FACTOR X (nM)
VIIIa/IXa STANDARD
IXa STANDARD
VIIIa+10nM DYDYQ(1,2)
VIIIa+25nM DYDYQ(1,2)
V0 (ARBITRARY UNITS)
FACTOR X (nM)

FIG. 11B

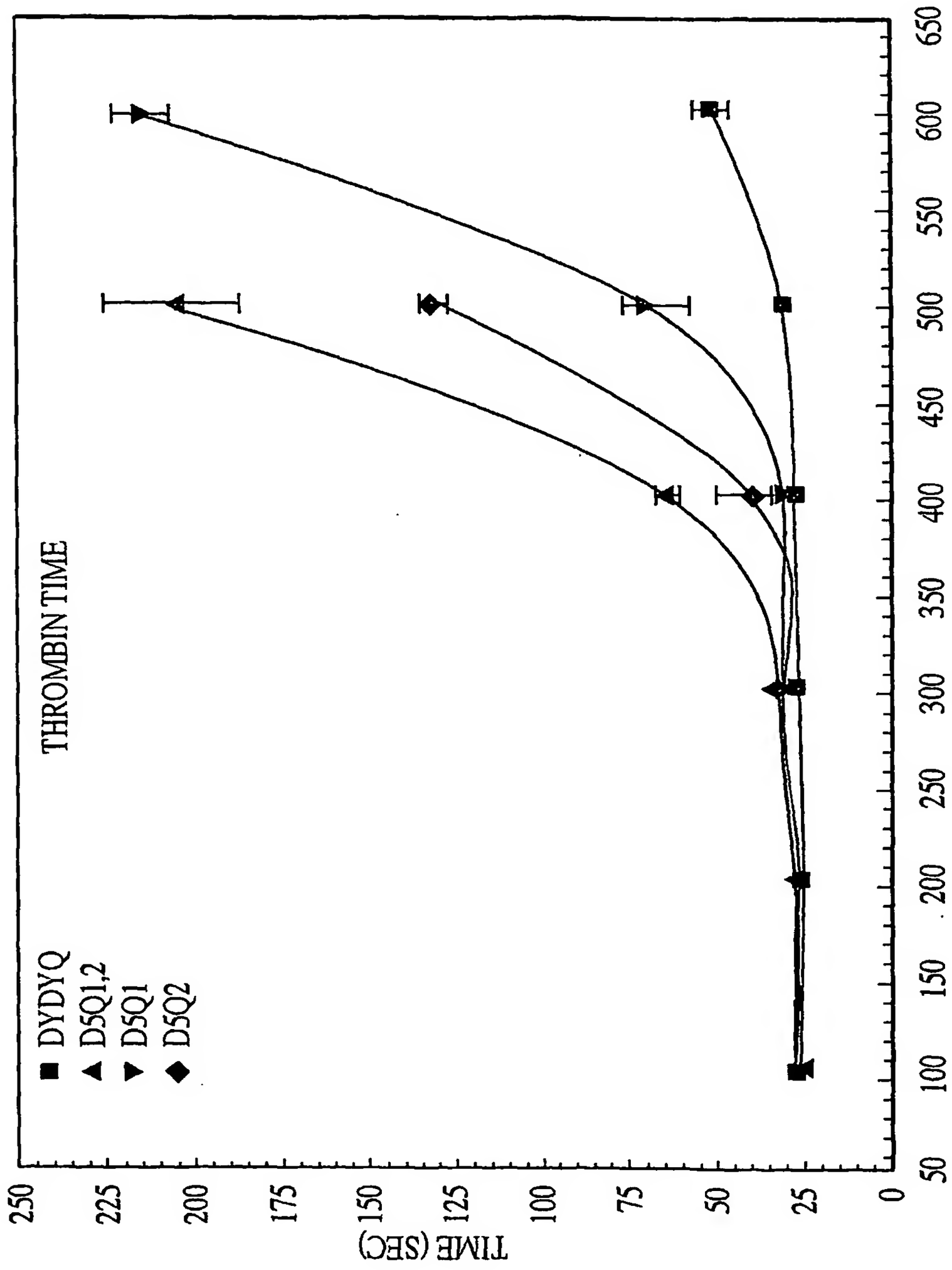

THROMBIN TIME
TIME (SEC)
PEPTIDE (μM)
DYDYQ
D5Q1,2
D5Q1
D5Q2
250
225
200
175
150
125
100
75
50
25
0
50
100
150
200
250
300
350
400
450
500
550
600
650

FIG. 12

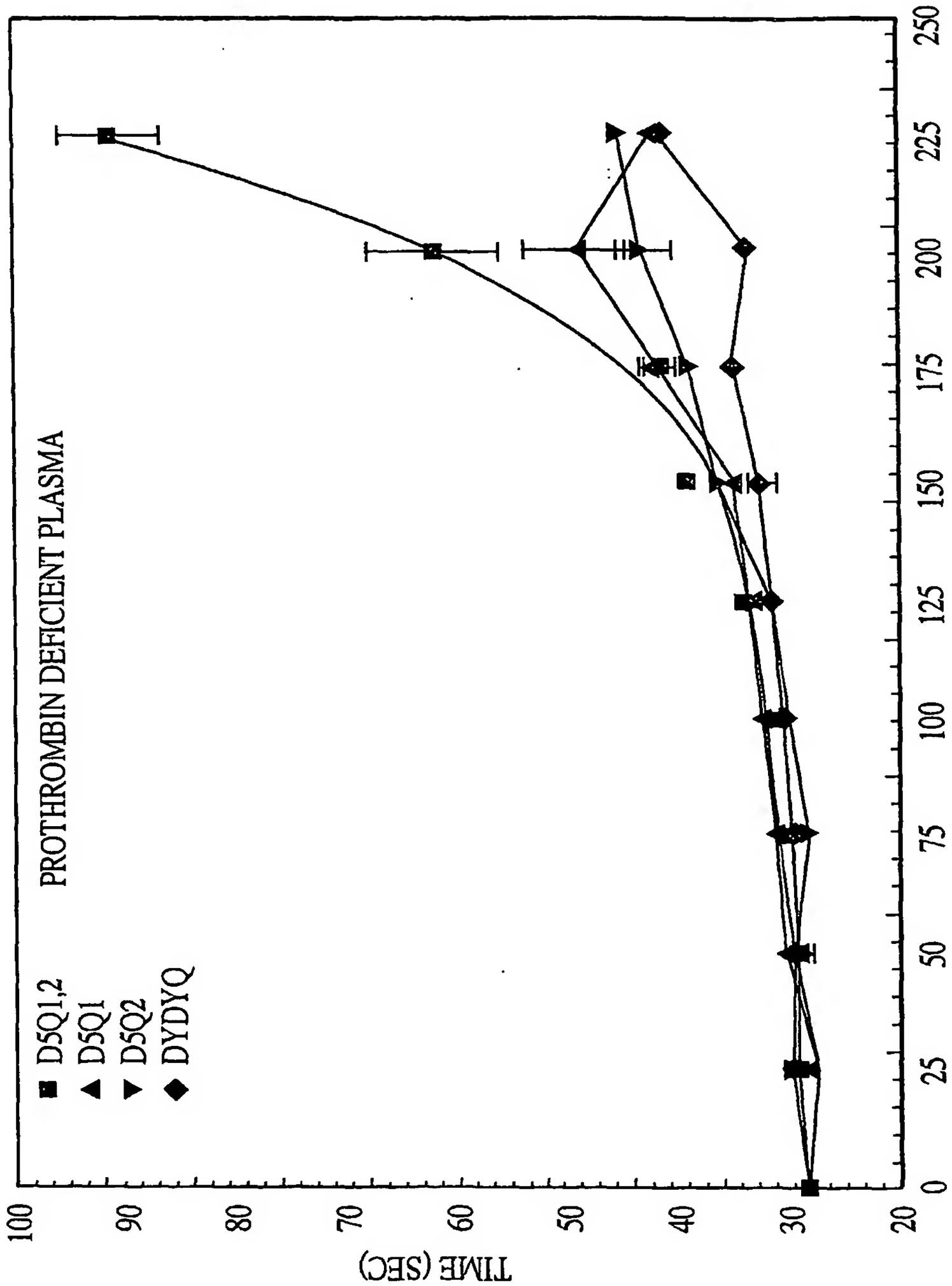

PROTHROMBIN DEFICIENT PLASMA
D5Q1,2
D5Q1
D5Q2
DYDYQ
TIME (SEC)
100
90
80
70
60
50
40
30
20
0
25
50
75
100
125
150
175
200
225
250
PEPTIDE (μM)

FIG. 13

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